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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
PAGONAKIS, ANNA	
ART UNIT	PAPER NUMBER
4173	

MAIL DATE	DELIVERY MODE
11/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/826,240	DUCHARME ET AL.	
	Examiner	Art Unit	
	Anna Pagonakis	4173	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2007*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *7-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8 sheets*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This is a supplemental office action. The previous office action mailed on 10/11/2007 is hereby vacated and the time for reply is restarted from the mailing of this office action.

Elections/Restrictions

Applicant's election with traverse of claims 1-6 in the reply filed on 9/10/2007 is acknowledged. Claims 7-12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected specie, there being no allowable generic or linking claim. Applicant timely traversed the restriction requirement in the reply filed on 9/10/2007. The traversal is on the grounds that the methods of Group II are searchable with Group I. This is not found persuasive because administering an angiotensin II receptor as in Group II is directed to a different mode of action. As stated in the restriction requirement inventions I and II are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects. Applicant's election with traverse of election requirement filed on 9/10/2007 is acknowledged. Applicant's traversal is on the grounds that all compounds have the same therapeutic result. This is not found persuasive because each specie has a unique mechanism of action in a biological system, and each specie claimed is patentably distinct, each from the other for the reasons stated in the last office action. Furthermore, the search of the entire groups in the non-patent literature (a significant part of thorough examination) would be burdensome.

The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

The information disclosure filed on 9/18/2007 has been received. Documents not provided were not considered during the examination process.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The use of the designation "ACE inhibitor" renders the claims indefinite as the recitation is too vague. "ACE" is a simple acronym/abbreviation that has many different meanings in the art and thus the inclusion thereof is confusion and the claims indefinite. Applicant could simply spell out the full name of the receptor in at least the first occurrence to obviate this rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification while being enabling for a decrease in the incidence of symptomatic or asymptomatic left ventricular systolic dysfunction, does not reasonably provide enablement for total prevention of symptomatic or asymptomatic left ventricular systolic dysfunction. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2nd 1400 at 1404 (CAFC 1988). A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification at the time of the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. The factors to be considered in determining whether undue experimentation is required include:

1. The nature of the invention

2. The breadth of the claims

3. The state of the prior art

4. The level of predictability in the art

5. The amount of direction provided by the inventors

6. The existence of working examples

7. The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

1. The Nature of the Invention

All of the rejected claims are drawn to a method of preventing the incidence of atrial fibrillation, specifically left ventricular systolic dysfunction, in a subject with chronic heart failure comprising administering a therapeutically effective amount of angiotensin-converting enzyme inhibitor (ACE). The nature of the invention is extremely complex in that it encompasses the actual prevention of the incidence of atrial fibrillation such that the subject treated with an ACE inhibitor does not even suffer from incidence of atrial fibrillation. Please note when prevention is supposed to never occur in the first instant. Early intervention with ACE inhibitors has been demonstrated to slow the progress of left ventricular enlargement and reduce morbidity and mortality. However, it is likely that selective administration of these drugs would be effective in responsive patient populations, but the criteria for identifying these populations are not yet available.

2. The breadth of the claims

Claims 1-6 are drawn to prevention of symptomatic or asymptomatic left ventricular systolic dysfunction. The scope of the claim is seen to include prevention of atrial fibrillation and the administration of said compound in an amount of 5-20 mg/day.

3. The state of the prior art

The examiner notes the prior art, "Effect of Enalapril on Mortality and the Development of Heart Failure in Asymptomatic Patients with Reduced Left Ventricular Ejection Fractions," discloses a decrease in the incidence of heart failure and the rate of related hospitalizations, as compared with the rates in the group given placebo (page 685, abstract). The prior art appears to be silent with regard to total preventive procedures recognized by skilled artisans in the field.

4. The level of predictability in the art

There is not sufficient data to substantiate the assertion that total prevention of left ventricular systolic dysfunction is possible by the use of the compound instantly claimed. The lack of significant guidance from the specification or prior art with regard to the actual prevention early intervention with ACE inhibitors has been demonstrated to slow the progression of left ventricular enlargement and reduce morbidity and mortality. However, it is likely that selective administration of these drugs would be effective in responsive patient populations, but the criteria for identifying these populations are not yet available. Heart failure is a progressive and lethal disease. Applicants' own disclosure states that "significantly less patients developing AF with enalapril (8 patients, 4.5%) than placebo (40 patients (23%); $p<0.0001$)" (page 9 of specification). Therefore, applicant's disclosure does not support that prevention of atrial fibrillation using enalapril occurred in all the patients.

Based on the prior art disclosure above and the said treatments, prevention is highly unpredictable.

5. The amount of direction provided by the inventor

The instant specification is not seen to provide enough guidance that would allow a skilled artisan to extrapolate from the disclosure and the examples provided to enable the use of the active agents for prevention of atrial fibrillation and specifically left ventricular systolic dysfunction.

6. The existence of working examples

The working examples set forth in the instant specification are drawn to prevention of atrial fibrillation and specifically left ventricular systolic dysfunction using the claimed compound. There are no examples using human or animal models that show the treatment and total prevention of any conditions as instantly claimed.

7. The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Indeed, in view of the information set forth, the instant disclosure is not seen to be sufficient to enable the total prevention of atrial fibrillation and specifically left ventricular systolic dysfunction. A skilled artisan would have to perform undue experimentation of the use of the compounds as instantly claimed with regard to the type of disorder/condition, dosage, frequency of dosage etc.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Nicklas et al. (New England Journal of Medicine, 1992, Vol. 327, page 685-691).

The above reference teaches with regard to instant claim 1, 4 and 6 the effect of ACE inhibitor, enalapril, on the development of heart failure in asymptomatic left ventricular dysfunction as in instant claim 2 and 3 (see methods, organization of the study) wherein the ACE inhibitor is administered in a dosage of 2.5 mg twice daily and was later increased to 10 mg twice daily as in instant claim 5 (see methods, eligibility of patients, run-in period and randomization).

Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Soeki T. et al. (Japanese Heart Journal, 1998, Vol. 39. No. 6, page 743-51).

Soeki et al. teaches the long term effects of the ACE inhibitor enalapril to patients with chronic heart disease. The study further states that one of the cause of heart failure was atrial fibrillation, ant that there was an improvement of left ventricular ejection fractions. Furthermore, the reference teaches that patients were administered 2.5-5.0 mg of enalapril once a day.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bourassa et al. (JACC, 1993, vol. 22, no. 4, pages 14A-19A) in view of Nicklas et al. (New England Journal of Medicine, 1992, Vol. 327, page 685-691.

Bourassa et al. on page 18A, right column under "Drug Therapy" teaches that 30 of patients studied received an ACE inhibitor and that because "these drugs prevent heart failure and prolong survival, they will undoubtedly be used more frequently in these patients in the future."

As mentioned above, Nicklas et al. teaches the use of enalapril to treat heart failure. Given what is taught in Bourassa et al. there is a clear motivation in the prior art to administer an ACE inhibitor such as enalapril taught by Nicklas et al. to patients with heart failure or left ventricular dysfunction.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anna Pagonakis whose telephone number is 571-270-3505. The examiner can normally be reached on Monday thru Thursday, 9am to 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

10/16/07

ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER